

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

***** Welcome to STN International *****

| | | | |
|------|----|--------|--|
| NEWS | 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS | 2 | JAN 02 | STN pricing information for 2008 now available |
| NEWS | 3 | JAN 16 | CAS patent coverage enhanced to include exemplified prophetic substances |
| NEWS | 4 | JAN 28 | USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats |
| NEWS | 5 | JAN 28 | MARPAT searching enhanced |
| NEWS | 6 | JAN 28 | USGENE now provides USPTO sequence data within 3 days of publication |
| NEWS | 7 | JAN 28 | TOXCENTER enhanced with reloaded MEDLINE segment |
| NEWS | 8 | JAN 28 | MEDLINE and LMEEDLINE reloaded with enhancements |
| NEWS | 9 | FEB 08 | STN Express, Version 8.3, now available |
| NEWS | 10 | FEB 20 | PCI now available as a replacement to DPCI |
| NEWS | 11 | FEB 25 | IFIREF reloaded with enhancements |
| NEWS | 12 | FEB 25 | IMSPRODUCT reloaded with enhancements |
| NEWS | 13 | FEB 29 | WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification |
| NEWS | 14 | MAR 31 | IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats |
| NEWS | 15 | MAR 31 | CAS REGISTRY enhanced with additional experimental spectra |
| NEWS | 16 | MAR 31 | CA/Caplus and CASREACT patent number format for U.S. applications updated |
| NEWS | 17 | MAR 31 | LPCI now available as a replacement to LDPCI |
| NEWS | 18 | MAR 31 | EMBASE, EMBAL, and LEMBASE reloaded with enhancements |
| NEWS | 19 | APR 04 | STN AnaVist, Version 1, to be discontinued |
| NEWS | 20 | APR 15 | WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats |
| NEWS | 21 | APR 28 | EMBASE Controlled Term thesaurus enhanced |
| NEWS | 22 | APR 28 | IMSRESEARCH reloaded with enhancements |
| NEWS | 23 | MAY 30 | INPAFAMDB now available on STN for patent family searching |
| NEWS | 24 | MAY 30 | DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option |
| NEWS | 25 | JUN 06 | EPFULL enhanced with 260,000 English abstracts |
| NEWS | 26 | JUN 06 | KOREAPAT updated with 41,000 documents |
| NEWS | 27 | JUN 13 | USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications |
| NEWS | 28 | JUN 19 | CAS REGISTRY includes selected substances from web-based collections |
| NEWS | 29 | JUN 25 | CA/Caplus and USPAT databases updated with IPC reclassification data |
| NEWS | 30 | JUN 30 | AEROSPACE enhanced with more than 1 million U.S. patent records |
| NEWS | 31 | JUN 30 | EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated |

organizations
 NEWS 32 JUN 30 STN on the Web enhanced with new STN AnaVist
 Assistant and BLAST plug-in
 NEWS 33 JUN 30 STN AnaVist enhanced with database content from EPFULL
 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
 AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.
 NEWS HOURS STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN Welcome Banner and News Items
 NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
 specific topic.

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 agreement. Please note that this agreement limits use to scientific
 research. Use for software development or design or implementation
 of commercial gateways or other similar uses is prohibited and may
 result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 08:59:51 ON 07 JUL 2008

=> file reg
 COST IN U.S. DOLLARS SINCE FILE TOTAL
 ENTRY SESSION
 FULL ESTIMATED COST 0.21 0.21

FILE 'REGISTRY' ENTERED AT 09:00:16 ON 07 JUL 2008
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
 provided by InfoChem.

STRUCTURE FILE UPDATES: 6 JUL 2008 HIGHEST RN 1032827-24-9
 DICTIONARY FILE UPDATES: 6 JUL 2008 HIGHEST RN 1032827-24-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when
 conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
 predicted properties as well as tags indicating availability of
 experimental property data in the original document. For information
 on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

=> E "EPOTHILONE B"/CN 25
 E1 1 EPOTHILONE A8/CN
 E2 1 EPOTHILONE A9/CN
 E3 1 --> EPOTHILONE B/CN
 E4 1 EPOTHILONE B (12R,13R) ACETONIDE/CN
 E5 1 EPOTHILONE B A-EPOXIDE/CN
 E6 1 EPOTHILONE B ACID/CN

| | | |
|-----|---|---|
| E7 | 1 | EPOTHILONE B HYDROXYLASE/CN |
| E8 | 1 | EPOTHILONE B HYDROXYLASE (AMYCOLATOPSIS ORIENTALIS GENE EBH)/CN |
| E9 | 1 | EPOTHILONE B N-OXIDE/CN |
| E10 | 1 | EPOTHILONE B10/CN |
| E11 | 1 | EPOTHILONE C/CN |
| E12 | 1 | EPOTHILONE C BIS(TERT-BUTYLDIMETHYLSILYL) ETHER/CN |
| E13 | 1 | EPOTHILONE C/D 12,13-EPOXIDASE/CN |
| E14 | 1 | EPOTHILONE C/D MONOOXYGENASE/CN |
| E15 | 1 | EPOTHILONE C/D SYNTHETASE/CN |
| E16 | 1 | EPOTHILONE C1/CN |
| E17 | 1 | EPOTHILONE C2/CN |
| E18 | 1 | EPOTHILONE C3/CN |
| E19 | 1 | EPOTHILONE C4/CN |
| E20 | 1 | EPOTHILONE C5/CN |
| E21 | 1 | EPOTHILONE C6/CN |
| E22 | 1 | EPOTHILONE C7/CN |
| E23 | 1 | EPOTHILONE C8/CN |
| E24 | 1 | EPOTHILONE C9/CN |
| E25 | 1 | EPOTHILONE D/CN |

=> S E3

L1 1 "EPOTHILONE B"/CN

=> S L1 EXA SAM

SAMPLE IS IGNORED AS A SCOPE FOR THIS SEARCH

L2 1 "EPOTHILONE B"/CN

=> DIS L2 1 SAM

THE ESTIMATED COST FOR THIS REQUEST IS 1.04 U.S. DOLLARS

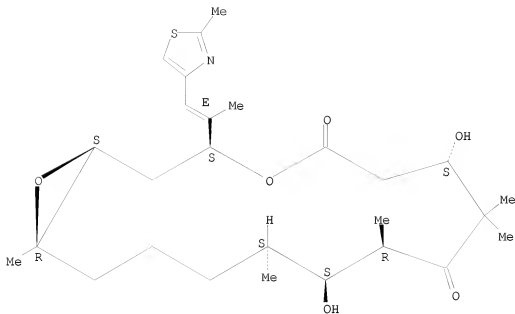
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN

IN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-
 8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-
 , (1S,3S,7S,10R,11S,12S,16R)-
 MF C27 H41 N O6 S

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

FULL ESTIMATED COST

ENTRY

SESSION

13.64

13.85

STN INTERNATIONAL LOGOFF AT 09:03:08 ON 07 JUL 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

***** Welcome to STN International *****

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 NEWS 2 JAN 02 STN pricing information for 2008 now available
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 of publication
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 NEWS 31 JUN 30 EMBASE, EMBAL, and LEMBASE updated with additional
 options to display authors and affiliated
 organizations
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 Assistant and BLAST plug-in
 NEWS 33 JUN 30 STN AnaVist enhanced with database content from EPFULL
 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
 AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.
 NEWS HOURS STN Operating Hours Plus Help Desk Availability
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 NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that

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* * * * * STN Columbus * * * * *

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=> file pctfull
COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                               ENTRY      SESSION
FULL ESTIMATED COST          0.21      0.21
```

FILE 'PCTFULL' ENTERED AT 10:10:27 ON 07 JUL 2008
COPYRIGHT (C) 2008 Univentio

FILE LAST UPDATED: 4 JUL 2008 <20080704/UP>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW FIELD UPTX, FIELD /EW NO LONGER AVAILABLE - SEE HELP CHANGE <<<

```
=> s epothilon?
L1      2484 EPOTHILON?
```

```
=> s l1/ab or l1/ti
        144 EPOTHILON?/AB
        129 EPOTHILON?/TI
L2      159 (EPOTHILON?/AB) OR (EPOTHILON?/TI)
```

```
=> s l2 not py>2001
        817323 PY>2001
L3      53 L2 NOT PY>2001
```

```
=> s combination and l3
        567168 COMBINATION
        264042 COMBINATIONS
        617900 COMBINATION
        (COMBINATION OR COMBINATIONS)
L4      33 COMBINATION AND L3
```

=> d ibib 1-5

```
L4      ANSWER 1 OF 33      PCTFULL  COPYRIGHT 2008 Univentio on STN
ACCESSION NUMBER:          2001092255 PCTFULL  ED 20020826
TITLE (ENGLISH):           EPOTHILONE DERIVATIVES AND METHODS FOR MAKING
                           AND USING THE SAME
TITLE (FRENCH):            DERIVES D'EPOTHILONE, PROCEDES DE PRODUCTION
                           ET METHODES D'UTILISATION
INVENTOR(S):               SANTI, Daniel;
                           FARDIS, Maria;
                           ASHLEY, Gary
PATENT ASSIGNEE(S):        KOSAN BIOSCIENCES, INC.;
                           SANTI, Daniel;
                           FARDIS, Maria;
                           ASHLEY, Gary
DOCUMENT TYPE:              Patent
```

PATENT INFORMATION:

| | NUMBER | KIND | DATE |
|--------------------|---|------|----------|
| DESIGNATED STATES | WO 2001092255 | A2 | 20011206 |
| W: | AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG | | |
| PRIORITY INFO.: | US 2000-60/207,655 20000526 US 2000-60/218,260 20000714 US 2000-60/231,552 20000911 | | |
| APPLICATION INFO.: | WO 2001-US15763 | A | 20010515 |

L4 ANSWER 2 OF 33 PCTFULL COPYRIGHT 2008 Univention on STN

ACCESSION NUMBER: 2001083800 PCTFULL ED 20020826

TITLE (ENGLISH): PRODUCTION OF POLYKETIDES

TITLE (FRENCH): PRODUCTION DE POLYKETIDES

INVENTOR(S): ARSLANIAN, Robert, L.;

ASHLEY, Gary;

FRYKMAN, Scott;

JULIEN, Bryan;

KATZ, Leonard;

KHOSLA, Chaitan;

LAU, Janice;

LICARDI, Peter, J.;

REGENTIN, Rika;

SANTI, Daniel;

TANG, Li

PATENT ASSIGNEE(S): KOSAN BIOSCIENCES, INC.;

ARSLANIAN, Robert, L.;

ASHLEY, Gary;

FRYKMAN, Scott;

JULIEN, Bryan;

KATZ, Leonard;

KHOSLA, Chaitan;

LAU, Janice;

LICARDI, Peter, J.;

REGENTIN, Rika;

SANTI, Daniel;

TANG, Li

DOCUMENT TYPE: Patent

PATENT INFORMATION:

| | NUMBER | KIND | DATE |
|-------------------|---|------|----------|
| DESIGNATED STATES | WO 2001083800 | A2 | 20011108 |
| W: | AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG | | |
| PRIORITY INFO.: | US 2000-09/560,367 20000428 US 2000-60/232,696 20000914 US 2000-60/257,517 20001221 | | |

US 2001-09/825,856 20010403
 US 2001-09/825,876 20010403
 US 2001-60/269,020 20010413
 APPLICATION INFO.: WO 2001-US13793 A 20010426

L4 ANSWER 3 OF 33 PCTFULL COPYRIGHT 2008 Univentio on STN
 ACCESSION NUMBER: 2001081341 PCTFULL ED 20020826
 TITLE (ENGLISH): 9-OXA-EPOTHILON DERIVATIVES, METHOD FOR THE
 PRODUCTION AND USE THEREOF IN PHARMACEUTICAL
 PREPARATIONS
 TITLE (FRENCH): DERIVES DE 9-OXA-EPOTHILONE, LEUR PROCEDE DE
 PRODUCTION ET LEUR UTILISATION PHARMACEUTIQUE
 INVENTOR(S): SCHWEDE, Wolfgang;
 KLAR, Ulrich;
 SKUBALLA, Werner;
 BUCHMANN, Bernd;
 HOFFMANN, Jens;
 LIGHTNER, Rosemarie
 PATENT ASSIGNEE(S): SCHERING AKTIENGESSELLSCHAFT;
 SCHWEDE, Wolfgang;
 KLAR, Ulrich;
 SKUBALLA, Werner;
 BUCHMANN, Bernd;
 HOFFMANN, Jens;
 LIGHTNER, Rosemarie
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2001081341 | A2 | 20011101 |

DESIGNATED STATES
 W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
 CZ DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
 JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
 MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
 TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL
 SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE
 DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG
 CI CM GA GN GW ML MR NE SN TD TG
 DE 2000-100 20 899.1 20000420
 WO 2001-EP4551 A 20010419

L4 ANSWER 4 OF 33 PCTFULL COPYRIGHT 2008 Univentio on STN
 ACCESSION NUMBER: 2001073103 PCTFULL ED 20020822
 TITLE (ENGLISH): PREPARATION OF EPOTHILONE INTERMEDIATES
 TITLE (FRENCH): PREPARATION D'INTERMEDIAIRES D'EPOTHILONE
 INVENTOR(S): VITE, Gregory, D.;
 KIM, Soong-Hoon;
 HOEFLE, Gerhard
 PATENT ASSIGNEE(S): BRISTOL-MYERS SQUIBB COMPANY;
 VITE, Gregory, D.;
 KIM, Soong-Hoon;
 HOEFLE, Gerhard
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2001073103 | A2 | 20011004 |

DESIGNATED STATES
 W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
 CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL
 IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG

MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ
 TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ
 SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH
 CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ
 CF CG CI CM GA GN GW ML MR NE SN TD TG

PRIORITY INFO.: US 2000-60/191,975 20000324
 APPLICATION INFO.: WO 2001-US9620 A 20010323

L4 ANSWER 5 OF 33 PCTFULL COPYRIGHT 2008 Univentio on STN
 ACCESSION NUMBER: 2001070716 PCTFULL ED 20020822
 TITLE (ENGLISH): A PROCESS FOR THE PREPARATION OF EPOTHILONE
 ANALOGS AND INTERMEDIATES
 TITLE (FRENCH): PREPARATION D'ANALOGUES ET D'INTERMEDIAIRES D'
 EPOTHILONE
 INVENTOR(S): LI, Wen, Sen;
 THORNTON, John, E.;
 GUO, Zhenrong;
 SWAMINATHAN, Shankar;
 MCONLOGUE, Gary, W.
 PATENT ASSIGNEE(S): BRISTOL-MYERS SQUIBB COMPANY;
 LI, Wen, Sen;
 THORNTON, John, E.;
 GUO, Zhenrong;
 SWAMINATHAN, Shankar;
 MCONLOGUE, Gary, W.
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| | NUMBER | KIND | DATE |
|-------------------|---------------|------|----------|
| DESIGNATED STATES | WO 2001070716 | A1 | 20010927 |

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
 CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
 MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
 TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
 SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
 DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
 CG CI CM GA GN GW ML MR NE SN TD TG

PRIORITY INFO.: US 2000-09/528,526 20000320
 APPLICATION INFO.: WO 2001-US7749 A 20010312

=> d his

(FILE 'HOME' ENTERED AT 10:09:50 ON 07 JUL 2008)

FILE 'PCTFULL' ENTERED AT 10:10:27 ON 07 JUL 2008

L1 2484 S EPOTHILON?
 L2 159 S L1/AB OR L1/TI
 L3 53 S L2 NOT PY>2001
 L4 33 S COMBINATION AND L3

=> s l4 and (taxol or paclitaxel)
 9622 TAXOL
 272 TAXOLS
 9705 TAXOL
 (TAXOL OR TAXOLS)
 10390 PACLITAXEL
 72 PACLITAXELS
 10392 PACLITAXEL
 (PACLITAXEL OR PACLITAXELS)

L5 29 L4 AND (TAXOL OR PACLITAXEL)

=> s 15 and Her?
988529 HER?

L6 29 L5 AND HER?

=> s 15 and (HER2 or HER-2)
4722 HER2
118696 HER
1043 HERS
119313 HER
(HER OR HERS)

1276185 2
3260 HER-2
(HER(W)2)

L7 1 L5 AND (HER2 OR HER-2)

=> d ibib abs

L7 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2008 Univentio on STN
ACCESSION NUMBER: 1999002514 PCTFULL ED 20020515
TITLE (ENGLISH): EPOTHILONE DERIVATIVES
TITLE (FRENCH): DERIVES D'EPOTHILONE
INVENTOR(S): VITE, Gregory, D.;
BORZILLERI, Robert, M.;
KIM, Soong-Hoon;
JOHNSON, James, A.

PATENT ASSIGNEE(S): BRISTOL-MYERS SQUIBB COMPANY
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

| NUMBER | KIND | DATE |
|------------|------|----------|
| ----- | | |
| WO 9902514 | A2 | 19990121 |

DESIGNATED STATES

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE
ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM
KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE
CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ
CF CG CI CM GA GN ML MR NE SN TD TG

PRIORITY INFO.: US 1997-60/051,951 19970708
US 1997-60/067,524 19971204
APPLICATION INFO.: WO 1998-US12550 A 19980616

ABEN The present invention relates to compounds of formula (I), Q is selected from the group consisting of (II), G is selected from the group consisting of alkyl, substituted alkyl, substituted or or unsubstituted aryl, heterocyclo, (III), W is O or NR15; X is O or H,H; Y is selected from the group consisting of O; H,OR16; OR17,OR17; NOR18; H,NOR19; H,NR20R21; H,H; or CHR22; OR17OR17 can be a cyclic ketal; Z1 and Z2 are selected from the group consisting of CH2, O, NR23, S or SO2, wherein only one of Z and Z2 is a heteroatom; B1 and B2 are selected from the group consisting of OR24, or OCOR25, or 2CNR26R27; when B1 is H and Y is OH, H they can form a six-membered ring ketal or acetal; D is selected from the group consisting of NR28R29, NR30COR31 or saturated heterocycle R1, R2, R3, R4, R5, R6, R7, R13, R14, R18, R19, R20, R21, R22, R26 and R27 are

selected from the group H, alkyl, substituted alkyl, or aryl and when R1 and R2 are alkyl can be joined to form a cycloalkyl; R3 and R4 are alkyl can be joined to form a cycloalkyl; R9, R10, R16, R17, R24, R25, and R31 are selected from the group H, alkyl, or substituted alkyl; R8, R11, R12, R28, R30, R32, R33, and R30 are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, or heterocyclo; R15, R23 and R29 are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, heterocyclo, R32C=O, R33SO2, hydroxy, O-alkyl or O-substituted alkyl, the pharmaceutically acceptable salts thereof and any hydrates, solvates or geometric, optical and stereoisomers thereof, with the proviso that compounds wherein: W and X are both O; and R1, R2, R7 are H; and R3, R4, R6, are methyl; and R8, is H or methyl; and Z1, and Z2, are CH2; and G is 1-methyl-2-(substituted-4-thiazolyl)ethenyl; and Q is as defined above are excluded.

ABFR La presente invention concerne des composés de la formule (I) dans laquelle Q est sélectionné dans le groupe constitué par le groupement (II); G est sélectionné dans le groupe constitué par alkyle, alkyle substitué, aryle substitué ou insubstitué, heterocyclo, le groupement (III); W est O ou NR15; X est O ou H; Y est sélectionné dans le groupe constitué par O; H, OR16; OR17, OR17; NOR18; H, NR19; H, NR20R21; H; ou CHR22; OR17, OR17 pouvant être un cétal cyclique; Z1 et Z2 sont sélectionnés dans le groupe constitué par CH2, O, NR23, S ou SO2, dans lequel seuls Z et Z2 sont un hétéroatome; B1 et B2 sont sélectionnés dans le groupe constitué par OR24 ou OCOR25 ou OCNR26R27; et peuvent former ensemble un noyau cétal ou acétal à six chaînons si B1 est H et Y est OH, H; D est sélectionné dans le groupe constitué par NR28R29, NR30COR31 ou un heterocycle saturé. R1, R2, R3, R4, R5, R6, R7, R13, R14, R18, R19, R20, R21, R22, R26 et R27 sont sélectionnés dans le groupe constitué par H, alkyle, alkyle substitué ou aryle, et peuvent former ensemble un cycloalkyle si R1 et R2 ou R3 et R4 sont alkyle; R9, R10, R16, R17, R24, R25 et R31 sont sélectionnés dans le groupe constitué par H, alkyle ou alkyle substitué; R8, R11, R12, R28, R30, R32, R33 et R30 sont sélectionnés dans le groupe constitué par H, alkyle, alkyle substitué, aryle, aryle substitué, cycloalkyle ou heterocyclo; R15, R23 et R29 sont sélectionnés dans le groupe constitué par H, alkyle, alkyle substitué, aryle, aryle substitué, cycloalkyle ou heterocyclo, R32C=O, R33SO2, hydroxy, O-alkyle ou O-alkyle substitué, leurs sels pharmaceutiquement acceptables ou leurs éventuels hydrates, solvates ou isomères géométriques, optiques, ou stéréoisomères, à condition que soient exclus les composés dans lesquels W et X sont tous deux O; et R1, R2 et R7 sont H; et R3, R4 et R6 sont méthyle; et R8 est H ou méthyle; et Z1 et Z2 sont CH2; et G est

1-methyl-2-(substitue-4-thiazolyl)ethenyle; et Q est tel que defini
ci-dessus.

=> d his

(FILE 'HOME' ENTERED AT 10:09:50 ON 07 JUL 2008)

FILE 'PCTFULL' ENTERED AT 10:10:27 ON 07 JUL 2008

L1 2484 S EPOTHILON?
L2 159 S L1/AB OR L1/TI
L3 53 S L2 NOT PY>2001
L4 33 S COMBINATION AND L3
L5 29 S L4 AND (TAXOL OR PACLITAXEL)
L6 29 S L5 AND HER?
L7 1 S L5 AND (HER2 OR HER-2)

=> s l6 and (HER2 or HER-2)

4722 HER2
118696 HER
1043 HERS
119313 HER
(HER OR HERS)
1276185 2
3260 HER-2

(HER(W)2)
L8 1 L6 AND (HER2 OR HER-2)

=> s l5 and (HER2 or HER-2)

4722 HER2
118696 HER
1043 HERS
119313 HER
(HER OR HERS)
1276185 2
3260 HER-2

(HER(W)2)
L9 1 L5 AND (HER2 OR HER-2)

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L9 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2008 Univentio on STN
ACCESSION NUMBER: 1999002514 PCTFULL ED 20020515
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TITLE (FRENCH): DERIVES D'EPOTHILONE
INVENTOR(S): VITE, Gregory, D.;
BORZILLERI, Robert, M.;
KIM, Soong-Hoon;
JOHNSON, James, A.
PATENT ASSIGNEE(S): BRISTOL-MYERS SQUIBB COMPANY
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| | CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ |
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ABEN The present invention relates to compounds of formula (I), Q is selected from the group consisting of (II), G is selected from the group consisting of alkyl, substituted alkyl, substituted or or unsubstituted aryl, heterocyclo, (III), W is O or NR15; X is O or H,H; Y is selected from the group consisting of O; H,OR16; OR17,OR17; NOR18; H,NOR19; H,NR20R21; H,H; or CHR22; OR17OR17 can be a cyclic ketal; Z1 and Z2 are selected from the group consisting of CH2, O, NR23, S or SO2, wherein only one of Z and Z2 is a heteroatom; B1 and B2 are selected from the group consisting of OR24, or OCOR25, or 2CNR26R27; when B1 is H and Y is OH, H they can form a six-membered ring ketal or acetal; D is selected from the group consisting of NR28R29, NR30COR31 or saturated heterocycle R1, R2, R3, R4, R5, R6, R7, R13, R14, R18, R19, R20, R21, R22, R26 and R27 are selected from the group H, alkyl, substituted alkyl, or aryl and when R1 and R2 are alkyl can be joined to form a cycloalkyl; R3 and R4 are alkyl can be joined to form a cycloalkyl; R9, R10, R16, R17, R24, R25, and R31 are selected from the group H, alkyl, or substituted alkyl; R8, R11, R12, R28, R30, R32, R33, and R30 are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, or heterocyclo; R15, R23 and R29 are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, heterocyclo, R32C=O, R33SO2, hydroxy, O-alkyl or O-substituted alkyl, the pharmaceutically acceptable salts thereof and any hydrates, solvates or geometric, optical and stereoisomers thereof, with the proviso that compounds wherein: W and X are both O; and R1, R2, R7 are H; and R3, R4, R6, are methyl; and R8, is H or methyl; and Z1, and Z2, are CH2; and G is 1-methyl-2-(substituted-4-thiazolyl)ethenyl; and Q is as defined above are excluded.

ABFR La presente invention concerne des composés de la formule (I) dans laquelle Q est sélectionnée dans le groupe constitué par le groupement (II); G est sélectionné dans le groupe constitué par alkyle, alkyle substitué, aryle substitué ou insubstitué, heterocyclo, le groupement (III); W est O ou NR15; X est O ou H,H; Y est sélectionné dans le groupe constitué par O; H,OR16; OR17,OR17; NOR18; H,NOR19; H,NR20R21; H,H; ou CHR22; OR17,OR17 pouvant être un cétal cyclique; Z1 et Z2 sont sélectionnés dans le groupe constitué par CH2, O, NR23, S ou SO2, dans lequel seuls Z et Z2 sont un hétéroatome; B1 et B2 sont sélectionnés dans le groupe constitué par OR24 ou OCOR25 ou 2CNR26R27; et peuvent former ensemble un noyau cétal ou acétal à six chaînons si B1 est H et Y est OH,H; D est sélectionné dans le groupe constitué par NR28R29, NR30COR31 ou un heterocycle saturé. R1, R2, R3,

R4, R5, R6, R7, R13, R14, R18, R19, R20, R21, R22, R26 et R27 sont selectionnees dans le groupe constitue par H, alkyle, alkyle substitue ou aryle, et peuvent former ensemble un cycloalkyle si R1 et R2 ou R3 et R4 sont alkyle; R9, R10, R16, R17, R24, R25 et R31 sont selectionnees dans le groupe constitue par H, alkyle ou alkyle substitue; R8, R11, R12, R28, R30, R32, R33 et R30 sont selectionnees dans le groupe constitue par H, alkyle, alkyle substitue, aryle, aryle substitue, cycloalkyle ou heterocyclo; R15, R23 et R29 sont selectionnees dans le groupe constitue par H, alkyle, alkyle substitue, aryle, aryle substitue, cycloalkyle ou heterocyclo, R32C=O, R33SO2, hydroxy, O-alkyle ou O-alkyle substitue, leurs sels pharmaceutiquement acceptables ou leurs eventuels hydrates, solvates ou isomeres geometriques, optiques, ou stereoisomeres, a condition que soient exclus les composés dans lesquels W et X sont tous deux O; et R1, R2 et R7 sont H; et R3, R4 et R6 sont methyle; et R8 est H ou methyle; et Z1 et Z2 sont CH2; et G est 1-methyl-2-(substitue-4-thiazolyl)ethenyle; et Q est tel que defini ci-dessus.

TIEN EPOTHILONE DERIVATIVES

TIFR DERIVES D'EPOTHILONE

DETD

R
S Me
jOH
N3], ']' '
O Me
O OH O
I EpothiloneA R=H
II EpothiloneB R=Me
have been found to exert microtubule-stabilizing effects similar to
TAXOL and hence cytotoxic activity against rapidly
proliferating cells,
such as, tumor cells or other hyperproliferative cellular disease, see
.Angew. Chem. Int. Ed. Engl., . . .

The compounds of this invention. are also useful in combination with known anti-cancer and cytotoxic agents and treatments, including radiation. If formulated as a fixed dose, such combination products employ the compounds of this invention within the dosage range described below and the other pharmaceutically active agent within its approved dosage range. Compounds of formula V can be used sequentially with known anticancer or cytotoxic agents and treatment, including radiation when a combination formulation is inappropriate.

Especially useful are cytotoxic drug combinations wherein the second drug chosen acts in a different phase of the cell cycle, e.g. S phase, than the present compounds of. . .

. . .
Synthase Inhibitors,
DNA Cross Linking Agents
Topoisomerase I and II Inhibitors
DNA Alkylating Agents

Ribonucleoside Reductase Inhibitors
Cytotoxic Factors e.g. TNF-alpha or
Growth factor inhibitors e.g. HER 2 receptor MAB's
The present compounds may exist as multiple optical, geometric,
and stereoisomers. Included within the present invention are all such
isomers and. . .

. . .
potency is
accomplished following a modified procedure of Swindell, et al., (see
Swindell, C.S., Krauss, N.E., Horwitz, S.B., and Ringel, I. Biologically
active taxol analogues with deleted A-ring side chain
substituents and
variable C-2' configurations. J. Med. Chem. 34: 1176-1184, 1991). These
modifications, in part, result. . .

. . .
cells were incubated at 37' for 72 hours at which time the
tetrazolium dye, MTS at 333 gg/ml (final concentration), in
combination
with the electron coupling agent phenazine methosulfate at 25 gm (final
concentration) was added. A dehydrogenase enzyme in live cells
reduces the MTS. . .

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

| | | |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 23.30 | 23.51 |

STN INTERNATIONAL LOGOFF AT 10:14:45 ON 07 JUL 2008